REMARKS

Claim 71 was amended to list individual types of drugs which are listed among others on page 18, beginning at line 18 and continuing to page 20, line 21. The process steps added to claim 71 as subparagraphs (a)-(e) are supported, for instance, in Example 1 on pages 23-24. In this example, as set forth beginning on line 24, the drug (doxorubicin) is (a) suspended in solvent with the components of the lipid/surfactant layer. This mixture is (b) evaporated and the evaporated mixture (c) dispersed into water. The fluorocarbon is then (d) added and the dispersion is (e) emulsified. This description is from lines 24-30 on page 23.

Claims 72-74 and 83-84 have been canceled to expedite prosecution as have claims 87-93. New claim 94 is a shorter list of drug types already contained in claim 71. Support for new claims 95-97 is found on page 18 at line 27 (claims 95-96) and on line 26 (claim 97). No new matter has been added and entry of the amendment is respectfully requested.

These amendments set forth the invention more clearly. The process steps added to claim 71 assure that the result in paragraph 4 of claim 71 is achieved, thus permitting the result in the last paragraph of the claim.

The Maintained Rejections

First, applicants wish to express their appreciation for the withdrawal of the rejection over Unger 2001/0018072.

Claim 71-19 and 82-86 were rejected as assertedly anticipated by U.S. 5,690,907; 5,780,010; or 5,958,371 as evidenced by three additional patents. The basis for this rejection is, in part, that set forth on page 3 of the Office action, last paragraph. This assumes that phosphatidyl ethanolamine is itself a drug. Applicants have already demonstrated that this is not the case, but in order to expedite

prosecution, the amendment to the claim clearly disposes of this aspect of the rejection. Whatever the effects of phosphatidyl ethanolamine, they do not place phosphatidyl ethanolamine into the categories of drugs to which claim 71 is now limited. Therefore, this aspect of the rejection is clearly overcome.

The other aspect of the rejection has to do with the naming of doxorubicin in the '907 patent as an example of a drug that might be incorporated into the particles. This aspect of the rejection is clearly not applicable to claims 95 and 96 which do not include doxorubicin. Respectfully, this aspect of the rejection is mistaken on several bases. First, subparagraphs (a)-(e) have been added to claim 1 requiring a particular procedure for ensuring that the drug is contained in the outer layer; these processes are never disclosed in the primary or secondary documents. Second, the reasoning set forth by the Office assumes that the nanoparticulate systems are "liposomes" citing U.S. 5,656,287 column 4, line 27. This location in the '287 patent simply says that in prior applications it was shown that liposome-encapsulated cyclosporin can be formulated having high entrapment characteristics along with good stability. How this demonstrates that the nanoparticles of the invention, which have a core consisting of liquid fluorocarbon coated with a lipid/surfactant layer, are liposomes escapes applicants.

In addition, the characteristics of the nanoparticles required by the claims is quite different from that of liposomes in precisely the manner that is significant to the argument made by the Office. The Office (at least in this part of the Office action) states that doxorubicin is a lipophilic drug that would have a tendency to incorporate into a lipid layer. This would indeed be the case, if doxorubicin itself is used, and if the composition is liposomal. Liposomes are particulates where a lipid bilayer surrounds an internal solution that is an aqueous solution and thus hydrophilic. Any

lipophilic drug would associate itself with the lipid bilayer instead of the internal compartment in liposomes. But the present nanoparticles do not have hydrophilic cores, they have hydrophobic cores and thus the argument falls. From the standpoint of hydrophobicity, the fluorocarbon cores and the lipid/surfactant coating are both hydrophobic (lipophilic). Thus, unlike the case for liposomes, with aqueous cores, lipophilic drugs are presented with both lipophilic layers and lipophilic cores. Accordingly, this maintained rejection should be withdrawn.

New Rejections

All claims were rejected as assertedly not enabled.

In direct contradiction to the argument made in the context of the above-maintained rejection, the Office appears to require "an explanation as to why a lipophilic drug will partition into the lipid layer and not into the liquid perfluorocarbon core." This explanation has been provided - it has already been explained on the record that conducting the steps set forth as (a) through (e) in claim 71 is necessary to assure that this is the case.

Applicants are confused by the assertion that possible drugs such as those that are anti-inflammatory, anti-rheumatic, etc., listed at the top of page 8 of the Office action are not supported in the specification. This appears to be a written description, not an enablement, argument and support for the classes of drugs in claim 71 in the specification has been identified hereinabove.

The remainder of the rejection asserts that as there are examples showing how both hydrophilic and lipophilic drugs could be incorporated into the lipid/surfactant layer, there is not sufficient enablement. It would appear that because of these illustrations, the specification teaches how a wide range of drug types could be incorporated into the lipid/surfactant layer.

The Office cites information from Kereos that drugs containing hydrophilic payloads are projected above the ligand-targeted emulsion surface and not contained within the layer. That is precisely why steps (a)-(e) are set forth in the claim, and taught in the specification to overcome this tendency.

Finally, having set forth the *Wands* factors, the Office fails to show any reason why these factors lead to the conclusion that the invention as claimed is not enabled. Accordingly, this basis for rejection may also be withdrawn.

Claims 71-79, 82-87, 89 and 92-93 were rejected as assertedly obvious over U.S. 5,690,907 in view of U.S. 4,595,680; 5,656,287; or 6,149,937.

With respect to the combination with '680, assertedly teaching that phosphatidyl ethanolamine is in fact a drug, this combination is no longer relevant, as phosphatidyl ethanolamine is no longer among the drugs included in the claims.

With respect to the combination with '937 and '287, the basis for the rejection appears to reside in the mistaken notion that the particulate carriers of the present invention are liposomes, which they are most assuredly not. Accordingly, this basis for rejection may also be withdrawn.

Conclusion

In light of the amendments to the claims and the foregoing remarks, it is believed that claims 71, 75-79, 82, 85-86 and 94-97 are in a position for allowance and passage of these claims to issue is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of

such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 532512000401.

Respectfully submitted,

Dated: December 11, 2007 By: / Kate H. Murashige /

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